CLINICIANS / GENETICS / CARE TEAMS

ASH1L clinician quick reference

A concise orientation, based on current evidence, for a first encounter, concern-directed review, or new functional change.

USE THIS WHEN

Preparing for a first encounter or reviewing a new change.

TIME NEEDED

Five-minute first read; keep with the chart.

TAKE OR SHARE

Use with the signed molecular report.

The diagnosis is relevant context, not a universal checklist.

Verify the molecular record, define baseline and the presenting concern, assess by clinical question, and avoid diagnostic overshadowing. Published and community evidence remain separate.

01 / EVIDENCE AND LIMITS

ASH1L at a glance

Statements below distinguish established gene-disease evidence from reported human features and unresolved clinical questions.

ESTABLISHED

Gene-disease relationship and inheritance

ClinGen classifies ASH1L as definitive for an autosomal dominant syndromic neurodevelopmental disorder. Haploinsufficiency has sufficient dosage evidence. Confirm the individual report rather than inferring consequence from gene name alone.

ESTABLISHED, WITH VARIANT-SPECIFIC LIMITS

Molecular mechanism

Loss of one functional copy is an established disease mechanism. Missense, splice, CNV/deletion, and complex consequences require variant-specific, transcript-aware interpretation.

SUPPORTED / HETEROGENEOUS

Human phenotype

Published reports support a heterogeneous neurodevelopmental phenotype. Individual features, severity, timing, and course cannot be inferred from the diagnosis alone; study-specific ascertainment and denominators matter.

CURRENT LIMIT

Management

No ASH1L-specific curative or disease-modifying treatment is established. Evaluate and manage presenting concerns using standard clinical practice, local guidance, and individualized supports.

Community information: information about 63 connected people, shared by individuals and families, is currently represented.

This is not a population sample. Molecular results are recorded for 62 of 63 people; one is pending. Recorded descriptions do not establish independent verification of every complete result.

02 / CLINICAL ORIENTATION

Published human evidence by concern

This is an evidence-orientation map, not a screening schedule. Published feature denominators remain attached to each source; absent systematic assessment limits inference.

ESTABLISHED CORE

Development, language, and adaptive function

Published case series consistently describe neurodevelopmental involvement, including developmental, language, intellectual, and adaptive differences. Severity and profile vary.

REPORTED / HETEROGENEOUS

Behavior and mental health

Neurobehavioral and psychiatric findings are reported. A diagnosis-specific prevalence estimate and the cause of a new behavior cannot be inferred from ASH1L alone.

REPORTED / INCOMPLETE

Seizures, EEG, spells, and sleep

Findings are reported across human sources with different ascertainment, definitions, and capture conditions. No single penetrance, EEG signature, or individual risk estimate is established.

REPORTED / UNEVENLY ASSESSED

Motor, tone, gait, feeding, GI, hearing, and growth

Selected findings appear in published cohorts, but these systems were not uniformly assessed. Review remains concern-directed and source-specific.

INSUFFICIENT FOR UNIVERSAL CLAIMS

Immune, cardiac, autonomic, endocrine, and other systems

Current evidence is insufficient to establish a universal ASH1L-specific syndrome, prevalence estimate, or screening pathway in these compartments.

03 / CLINICAL SEQUENCE

First encounter: five high-value moves

The aim is to define the person, the molecular record, the clinical question, and the evidence that could change the plan.

01

Verify the signed molecular report

Record transcript, exact cDNA and protein lines, classification, inheritance, method, limitations, and additional findings.

02

Define baseline and the reason for referral

Separate longstanding phenotype from a new change in function, comfort, behavior, or participation.

03

Assess by presenting concern

Avoid a universal ASH1L checklist. Apply standard differential diagnosis and concern-specific evaluation.

04

Plan access to care

Document communication, sensory, procedural, mobility, and pain-expression supports needed for a valid encounter or test.

05

Name uncertainty and the next discriminator

State what is known, what remains uncertain, and what observation, acquisition condition, or test could change the plan.

Negative results require acquisition context.

A normal study answers only the question it captured. Timing, sensitivity, technical quality, sleep or event capture, and the relevant clinical window determine what can reasonably be excluded.

04 / DIFFERENTIAL-FIRST REVIEW

When behavior or function changes

New behavior is clinical data. Keep pain, neurological state, physiology, medication, environment, communication, and recovery visible at the same time.

KEEP VISIBLE

Pain and bodily state

Dental, GI, urinary, musculoskeletal, headache, skin, menstrual, injury, or other pain sources.

KEEP VISIBLE

Neurology and sleep

Seizure or spell, acute focal concern, movement change, headache, sleep loss, or postictal/recovery state.

KEEP VISIBLE

Illness and physiology

Infection, hydration, nutrition, endocrine, autonomic, cardiopulmonary, or post-procedure state.

KEEP VISIBLE

Medication and exposure

Start, stop, dose or formulation change, interaction, anesthesia, supplement, or unintended exposure.

KEEP VISIBLE

Environment and communication

Sensory demands, demand mismatch, disrupted routine, communication access, trauma, or mental-health concern.

KEEP VISIBLE

Recovery and new baseline

Duration, completeness, recurrence, loss of prior baseline, and supports associated with restored access.

Escalate according to the clinical presentation.

Sudden weakness, loss of consciousness, breathing difficulty, prolonged or repeated seizures, serious injury, severe dehydration, or another unsafe change requires urgent evaluation under local guidance.

05 / MEASUREMENT AND REFERENCES

Document what makes the result interpretable

The report should preserve the clinical window, acquisition conditions, representative event capture, source, and recovery - not only a binary result.

PLAN

Before testing

Define the target question, representative state or event, baseline, timing, and supports required for valid acquisition.

DOCUMENT

In the report

State acquisition quality, sleep or event captured, limitations, original result wording, and what the method cannot answer.

INTERPRET NARROWLY

After testing

Link the result to the clinical question, next decision, recovery course, and any new baseline. Preserve competing explanations.

CLOSE THE LOOP

Communication

Name who will review results, how they will be shared, and when follow-up occurs. Avoid diagnostic overshadowing in the handoff.

Core references

1. ClinGen ASH1L gene-disease validity
https://search.clinicalgenome.org/kb/genes/HGNC%3A19088

2. ClinGen ASH1L dosage sensitivity
https://search.clinicalgenome.org/kb/gene-dosage/HGNC%3A19088

3. Cordova et al. Genes. 2024;15:423. doi:10.3390/genes15040423
https://doi.org/10.3390/genes15040423

4. Shen et al. Eur J Med Genet. 2019. doi:10.1016/j.ejmg.2018.05.003
https://doi.org/10.1016/j.ejmg.2018.05.003

5. Okamoto et al. Am J Med Genet A. 2017. doi:10.1002/ajmg.a.38193
https://doi.org/10.1002/ajmg.a.38193

Scope

This family-founded educational reference is not a clinical guideline, surveillance schedule, or independently validated standard of care. It avoids person-level histories and unsupported prevalence estimates.